fibrinogen are absent and blood serums or blood placquelets, will not give the desired results. In this condition it has the double effect of correcting the anemia and shortening the coagulation time.

The indications for transfusions may then be practically summed up in the following manner: It may be used in any condition to correct a very severe anemia or it may be the only method of rapidly controlling a lengthened coagulation time.

DIABETES INSIPIDUS.

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Our knowledge of diabetes insipidus at the present time is well examplified by the fact that of those who have given careful consideration to this pathological manifestation, some call it a "disease" while other authorities prefer to designate diabetes insipidus as a "disease syndrome." Diabetes insipidus is of comparatively rare occurrence, being about 14 in 100,000 patients. One therefore approaches each new case with interest, and with the hope of finding a clue to its etiology and proper treatment.

In a very interesting study, Fitz[1] calls attention to the fact that diabetes insipidus was recognized in 1682 by Thomas Willis, and well described by Johann Peter Frank in 1794, and it is remarkable that so little information has been gathered since that time. This, however, may be due to the fact that diabetes insipidus does not have a definite anatomical basis, or if it does, it certainly has escaped detection. In more recent times the problem of diabetes insipidus is being approached by the avenue of functional pathology, and results seem more promising.

Diabetes insipidus may be defined as a disease state characterized y an excessive polydipsia and polyuria.

According to various observers it has been known to occur when there was an hereditary tendency to the disease; it has been known to occur after fevers, after physical injury to the brain and cord, after psychic trauma, after luetic disease of the nervous system (particularly basilar meningitis), after tumor of the brain, and after tumor or irritation or injury to the hypophysis, such injury being accidental or following surgical interference, and also after injury to the temporal region of the brain, and particulrly after injury in the region of the floor of the fourth ventricle. Diabetes insipidus has been known to occur in cases of carcinoma of the liver and of the adrenals (by metastasis?), and in disease of the pancreas.

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[1] Arch. Int. Med., 1914, xiv, 706.

It will be of interest to cite the tendency of modern opinion held by those who have studied this condition. Allen[2] says: "In general there seems to be ground for believing that diabetes insipidus belongs among the disorders of internal secretion. The facts are not yet sufficient to warrant a conclusion or hypothesis."

Falta[3] states: "We must leave the genesis of the disease open." Fitz holds: "On the whole it appears that diabetes insipidus is usually of the symptomatic type, though it may be of the idiopathic. The exact cause of the polydipsia and polyuria is undetermined. Certain observers believe that the concentrative powers of the kidneys are at fault, others that the polyuria results from an abnormal thirst." Barker[4] likewise holds the view that there are two forms of this disease: the idiopathic diabetes insipidus, due to a functional disturbance of the kidney, which makes them incapable of secreting a concentrated urine, and the symptomatic diabetes insipidus, in which there is no functional insufficiency of the kidneys. The polyuria is secondary to a primary polydipsia, this latter type being of neurogenic origin or due to some disturbance of internal secretion.

The case reported by Fitz showed that the kidneys were capable of performing a normal amount of work, but there was a particular sensitiveness to salt. The ingestion of 25 grams of sodium chloride brought on a marked diuresis, "vascular hyposthenuria."

The case to be reported here will be presented from the standpoint of functional capacity of the kidney, whether the kidneys were hypersensitive to urea, chlorides, and glucose, and to record those other observations which time and circumstance permitted. Excepting for one day in the hospital the patient was an ambulatory case, and it required much tact to procure the observations which I was permitted to make, as he had already seen many physicians, and did not care to lend himself to extended observations.

Case History.—W. C. B., male, aged forty-eight years; family history is good; previous health good. No history of venereal disease, accident, or trauma. In August, 1912, had an attack which his physicians designated congestion of kidneys; recovery was good. Eighteen months ago, independent of everything else, he developed polydipsia and polyuria, but no polyphagia. Fourteen months ago had an attack of "grip," followed by exsiccation and exfoliation of skin and mucous membranes. Since the onset of polyuria he has been passing from 6 to 11 quarts of urine daily. Five years ago he weighed 175 pounds, six months ago 190 pounds, and now weighs 195 pounds; so that, irrespective of the polyuria, his body weight has increased and his nutrition is apparently unaffected.

He follows his occupation, cattle rancher, which entails much physical exertion, and frequently hardships. His diet is that of many American workmen, high in protein. He eats eggs, fruit, and coffee for breakfast; meat, vegetables, dessert, and coffee for luncheon; soup, meat, vegetables, coffee, and dessert for dinner. His physical comfort varies with his ability to get water.

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[2] Glycosuria and Diabetes, Harvard Univ. Press, 1913, p. 523.

[3] The Ductless Glandular Diseases, Blakiston, 1915, p. 323.

[4] Monographic Medicine, iv, 815.

In the foothills of the Rocky Mountains, for a distance of forty miles from the Main Divide, he nearly always manages to get a supply of good water while crossing streams, at least once in three hours. But when he gets in the low country, where the soil and the water are both rich in alkali, he suffers much inconvenience. The alkali water and the sulphur waters are undesirable for drinking, and with him, as with the other men, it frequently causes an irritability of the bladder.

Physical Examination. Height, 5 feet 6 inches; weight, 195 pounds; general type, robust. Skeleton and features normal. Head and neck negative. Vision normal. Radiograph shows a normal sella turcica. Chest: lungs negative, heart negative. Blood-pressure: maximum, 156; minimum, 97; pulse, 84. Abdomen negative. Extremities negative. Reflexes normal. Glands negative. Gastro-intestinal history negative. Nervous system negative. Circulatory history negative. Blood count normal. Wassermann negative. Urine shows trace of albumin; no casts.

Water Excretion. The patient did not lend himself to the water test, as his thirst seemed unsatiable. He would not or could not control the thirst sufficiently to permit a starting-point for the test, aside from the difficulty he would have had in taking an amount of water greater than he was already drinking.

His average excretion was 500 c.c. to 600 c.c. per hour.

Polydipsia. This was the patient's chief complaint, his inordinate desire for water, and it was, as he said, not because of his need for the water, which when it reached his stomach made him feel oppressed and uncomfortable, but that he craved the water to allay the horrible "leathery" taste in the roof of his mouth, pharynx, and back of his tongue. Abstinence from drinking made him feel that his parched tongue would stick to the roof of his mouth and the back of his throat." Even copious rinsing of the mouth did not relieve him. This parageusia may indicate an alteration in function or structure of the glossopharyngeal nerve or central involvement at the medulla. Blocking of that nerve would have been an important experiment in this case had it been possible.

Hyposthenuria. For a period of one month, during which the patient kept careful account of his daily urinary output, the maximum was 12,450 c.c. and the minimum 11,000 c.c., the average secretion being 11,670 c.c. per day. During a period of three days, on a constant diet, the patient received successively 20 grams of urea, 10 grams of salt, and 100 grams of glucose. After the urea he excreted 13,396 c.c., after the salt 13,110 c.c., and after the glucose

12,930 c.c.; so that in response to the increased presence of these substances in the blood we find there was greater demand for water and a larger urinary excretion.

Conversely, when the patient was placed on a Mosenthal salt-free diet the total excretion within the following twenty-four hours decreased promptly from 12,930 c.c. to 10,500 c.c., a fall of 2430 c.c. in twenty-four hours. How the kidneys responded to each one of the substances separately will be referred to later.

Specific Gravity. This varied between 1000 and 1003; the latter concentration was attained on the day the urea was taken.

Urea Excretion. In the twenty-four hours following the ingestion of urea the specific gravity rose from 1001 to 1003, and the entire 20 grams of urea were eliminated. This shows a definite ability on the part of the kidney to concentrate urine. The urinary output was 13,396 c.c., evidencing a greater than average desire for water and proportionate elimination. There was no hypersensitiveness to urea.

Salt Excretion. After 10 grams of salt given on the day following the urea the total volume of urine was slightly diminished; the specific gravity was 1001. The salt was eliminated promptly as the urea was, 9.4 grams in the twenty-four hours. There was no hypersensitiveness to salt.

Glucose. Four and a half hours after supper 100 grams of glucose were taken. This was followed by a diuresis of 2640 c.c., which kept him awake during the next four hours. A portion of this four-hour specimen of urine reacted positive to Benedict's, Almen-Nylander's bismuth test, and produced fermentation. Quantitatively, the amount was too small for estimation.

That glucose does not ordinarily produce a diuresis was shown by Taylor and Hulton,[5] who administered from 200 to 50) grams of glucose in twenty normals and rarely found a diuresis.

Hydrogen Ion Concentration of the Urine. As tested on several occasions I found to methyl orange the reaction was alkaline, to methyl red it was alkaline, to phenolphthalein acid and to Kahlbaum's neutral litmus it was slightly acid.

The hydrogen ion concentration of the urine may therefore be recorded as being 10 to 9, or about normal.

Salt-free Diet. Placing the patient on a Mosenthal salt-free diet resulted in a prompt decrease of 2400 c.c. urine during the following day. The salt elimination was moderately diminished and urea was decreased by exactly half of the previous day.

Phenolsulphonephthalein Output. Dye appeared in ten minutes. At the end of the first hour there was 600 c.c. of urine, specific gravity 1004, and dye elimination 16 per cent. Total phenolsulphonephthalein elimination, 69 per cent.

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[5] Taylor and Hulton, Jour. Biol. Chem., 1916, xxv, 173.

Lumbar Puncture. Upon entering the spinal canal the fluid came through the needle in a steady stream, which had not diminished when 25 c.c. was removed. I thought it inadvisable to remove more, and stopped. There was no increased pressure behind the flow, and I looked upon this as being one phase of the general flux of fluids in the body of this patient. This may prove to be an important observation that in some cases at least the greater liquid exchange is not limited to the kidney.

On the day preceding lumbar puncture the urinary output was 12,000 c.c.; on the following day, the patient having been kept in bed, it was 7950 c.c.; on the next day the patient was up and about, *and it was again 12,000 c.c.* Lumbar puncture had no more than a transitory if any influence upon the polyuria. No cells were to be found in the fluid. The globulin test was negative, sugar reaction slight, and the Wassermann in quantities of 0.2, 0.4, and 0.8 c.c. was negative. I now believe that we should have used much larger amounts of the spinal fluid as well as the blood for Wassermann tests on account of the high dilution of the body fluids.

Saliva. Upon examination of the mouth it was readily seen there was a copious salivary flow, as the saliva trickled down the inner cheek from the mouth of Stenson's duct in a continuous stream. The salivary secretion from the sublingual gland was likewise profuse. To Kahlbaum's neutral litmus the reaction was acid. We may account for the sialorrhea in several ways: (1) as with urinary flow and the spinal fluid, the liquid exchange or flow through organs which normally secrete a fluid is abnormally large; (2) that the sialorrhea is physiological and occurs in response to the parageusia through stimulation of the parotid gland; (3) that the sialorrhea is pathological and is the product of an abnormal stimulation or disease of the nerves governing the function of the gland, glossopharyngeal, or its centre in the medulla. The salivary glands are sensitive to stimulation, $\frac{1}{5}$ grain of pilocarpin markedly increased the already large flow of saliva.

Drugs. Without going into details of the pharmacological action of these drugs I merely note the effect of the following drugs:

Atropin, grain $\frac{1}{50}$ t. i. d. for four days, caused no change in amount nor concentration of urine.

Sodium nitrate, *gr. iij, q. i. d.,* no effect.

Potassium bromide, *gr. 10 q. i. d.,* no effect.

Pilocarpin, gr. $\frac{1}{5}$ produces a marked diuresis lasting two hours, during which time there is eliminated 500 to 1000 c.c., more urine than is normal for him. After two hours there is a decrease, also lasting two to three hours, after which time the normal rate of flow is resumed.

SUMMARY. A case of diabetes insipidus with kidneys capable of eliminating a normal amount of solids in the twenty-four hours. In response to ingestion of added amounts of salt and urea the kidneys show ability to eliminate these substances promptly and to concentrate urine. In response to the ingestion of 100 grams of glucose the urine showed a trace of sugar and a diuresis followed. Phenosulphonephthalein elimination was normal. There were evidences in this case suggesting that the abnormally large liquid exchange was not limited to the kidneys, but that the spinal fluid and saliva were likewise secreted in abnormally large amounts.

It was demonstrated that although the kidneys and salivary glands were already performing an inordinate amount of work, as far as excretion of water is concerned they were not functioning to their maximum capacity.

Pilocarpin produced a sialorrhea and diuresis after each dose on several days. Circumstances did not permit any attempt at determining the part played by the internal secretions in this case, nor was it possible to make any observations toward determining the part played by the glossopharyngeal nerve in the polydipsia.

THE METASTASIS OF TUMORS: A STUDY OF 298 CASES OF MALIGNANT GROWTH EXHIBITED AMONG 5155 AUTOPSIES AT BELLEVUE HOSPITAL.

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There are reasons for believing that as a result of accident or other fortuitous circumstance, or even in the ordinary course of events, certain fixed cells may become liberated into the circulation, *e. g.*, placental cells may be freed and transported to the liver, and liver cells may be released and carried to the lungs. In either event proliferation of the transplanted cell is obstructed not only by equilibrium of function in the cell itself, but by the innate antagonism of the tissue in which it finds lodgment. There are equally acceptable reasons for believing that the cells of certain tumors are more or less constantly discharged into the blood stream and destroyed. Seldom is this destructive property placed in abeyance, as is evidenced by the rarity of universally disseminated metastases in human tumors and by the low proportion of successful inoculations following injection into the blood stream of emulsions of the transplantable tumors of lower animals. The lymph stream, on the contrary, seems to be devoid of inimical properties, and the tumor cell, particularly the epithelial variety, not only